Alcohol Consumption and Breast Cancer Risk among Women under Age 45 Years

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In a population-based case-control study of women younger than 45 years of age, we obtained a detailed lifetime history of alcohol use to evaluate the effects of drinking during different periods of life in relation to breast cancer risk. This analysis focused on interviews obtained from 1,645 cases and 1,497 controls. Breast cancer risk was not influenced by drinking during the teenage years or early adulthood. Contemporary drinking (that is, average intake during the recent 5-year interval) was directly associated with risk, but the adverse effect of recent drinking was restricted to women who consumed ≥14 drinks per week [relative risk (RR) = 1.7; 95% confidence interval (CI) = 1.2–2.5]. The effect of alcohol was most pronounced among women with advanced disease. Compared with nondrinkers, the risk estimate associated with recent consumption of ≥14 drinks per week was 2.4 (95% CI = 1.6–3.8) for women with regional/distant disease. Our data add support to the accumulating evidence that alcohol consumption is associated with increased risk of breast cancer and further indicate that alcohol acts at a late stage in breast carcinogenesis. (Epidemiology 1997;8:231–237)

Keywords: alcohol drinking, breast neoplasms, case-control study, age.

Many epidemiologic studies indicate that alcohol consumption is related to breast cancer risk.[1,2] A number of issues regarding the relation remain unresolved, however. Few studies provide persuasive evidence of a dose-response gradient, leading to questions concerning the causality of the association. Some studies indicate that there is a threshold below which alcohol has no perceptible effect. This threshold, however, has been reported to range from a few drinks per week to as many as 3–4 drinks daily.[3–5] Although some studies indicate that breast cancer risk is influenced by the type of alcoholic beverage consumed, results are inconsistent.[2] Most studies have examined the effects of usual intake, which may actually more closely reflect recent consumption. Relatively few studies have assessed both contemporary and past intake. A report by Harvey *et al*[6] indicated stronger associations for drinking before age 30 years compared with later drinking. Several subsequent studies, however, have not confirmed associations with early drinking.[5,7–9]

We obtained a lifetime history of alcohol use in a large case-control study of young women, providing an opportunity to compare the effects of drinking during different periods of life.

Subjects and Methods

This population-based case-control study[10] was conducted in three geographic areas covered by cancer registries: the metropolitan areas of Atlanta, GA, and Seattle/Puget Sound, WA, and five counties of central New Jersey. The present analysis is based on women 20–44 years of age, who were newly diagnosed with *in situ* or invasive breast cancer during the period May 1, 1990, through December 31, 1992. Cases were identified through rapid ascertainment systems. Hospital records of eligible patients were abstracted to document details on the clinical and pathologic characteristics of the diagnosed breast cancers. Controls were frequency matched by geographic area and age to the expected distribution of cases and were identified through random digit dialing.[11] Of the 16,254 residential telephone numbers selected, 90.5% of the households agreed to a brief telephone screener interview used to identify potential controls.

Interviews were obtained from 1,501 of the 1,908 eligible controls (78.7%) and 1,668 of the 1,939 eligible

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cases (86.0%). Eighty-four per cent of cases were interviewed within 6 months of diagnosis. The major reasons for non-interview were subject refusals (12.9% in controls, 6.6% in cases) and physician refusals (5.8% of cases). Among the controls, the overall response rate was 71.2% (the interview response rate times the telephone screener rate). Because controls were identified through telephone sampling, 21 cases without residential telephones were eliminated from the analysis. Two cases and 4 controls did not provide information about alcohol use. This analysis focused on 1,645 cases and 1,497 controls.

Structured in-person interviews provided detailed information regarding known and suspected breast cancer risk factors, medical and breast cancer screening history, and certain life-style factors and opinions about cancer causation. Immediately after the interview, a variety of anthropometric measurements were made, including determinations of height and weight.

A lifetime history of alcohol use was obtained during the interview. The questionnaire was designed to address the relative importance of contemporary and past drinking. Rather than ask about usual intake during 10-year intervals, as is often done, questions about alcohol consumption were structured to allow respondents to account for life events (for example, adolescence, leaving the parental home, pregnancy) likely to be associated with changes in alcohol consumption.

Drinkers included women who reported that they had consumed at least 12 drinks of alcohol-containing beverages during their lifetime and had drunk at least once a month for 6 months or more. Women identified as drinkers were asked when they first drank alcoholic beverages. The age reported defined the beginning of their first drinking interval. They were then asked separate questions about frequency of consumption (times per day, week, month, or year) of beer (12-ounce bottle or can), wine (4-ounce glass), and liquor (1.5-ounce shot). After answering questions about all three types of alcohol-containing beverages, women were asked when their drinking habits changed. This age marked the beginning of the second drinking interval. The previous sequence of questions was repeated until the women reported no changes in drinking habits. The median number of drinking intervals reported by both cases and controls was three.

As a precaution against including changes in alcohol intake related to diagnosis or events leading to diagnosis, all alcohol exposure variables were truncated to diagnosis age (or age at the time of the random-digit-dialing telephone screening) minus 2 years. Hereafter, the truncation date is referred to as the reference date. Usual intake of alcohol was defined as average intake from the start of drinking up to the reference date. We defined recent intake as average consumption for the 5-year period leading up to the reference date. To assess past drinking, we calculated average intake for women when they were in their teens, twenties, and thirties.

We used logistic regression to obtain relative risk (RR) estimates and their 95% confidence intervals (CIs),[12] adjusted for potential confounders. We evaluated trend in the logistic analyses by categorizing the ordinal exposure variable, coding it as (1, 2, 3, etc) and treating the scored variable as continuous, after eliminating unknown values. We used the technique of cubic splines to estimate a smoothed dose-response curve plotting recent alcohol consumption, as a continuous variable, against RR. Specifically, we used the natural spline function(s) of S-Plus[13] which adequately fit the data based on chi square tests of deviance with the fewest degrees of freedom. In analyses involving stage of diagnosis as an outcome, we used polychotomous logistic regression to compare each case group simultaneously with the controls.[14]

Results

The median age of cases was 40 years, and that of the controls was 39 years. Both groups were 79% white, 15% black, and 6% other races. Socioeconomic status, as measured by education and income, was similar for both groups (data not shown). The distribution of cases and controls according to family history of breast cancer, a previous breast biopsy report, reproductive/menstrual history, and body size was compatible with the recognized risk profile for young women with breast cancer (Table 1).

Among controls, women who consumed alcohol tended to be younger, more often white, better educated, and more frequent users of oral contraceptives; they also tended to have fewer births and a later age at first birth compared with nondrinkers (data not shown). Controls who consumed alcohol also tended to be taller and thinner and were more likely to be current or former smokers. In addition to the matching factors of age and study site, we included race (white, black, other), oral contraceptive use (no, yes), and parity (0, 1, 2, 3, ≥4) as potential confounders in logistic analyses for alcohol relations. Addition of other variables [for example, family history, previous breast biopsy, age at first birth, height, body mass index [BMI; weight (kg) per height squared (m^2)], and smoking status] did not materially alter the risk estimates for alcohol effects.

Risk of breast cancer was only slightly higher (RR = 1.1; 95% CI = 1.0–1.3) among drinkers compared with nondrinkers. To assess the effect of the amount of alcohol consumed, we evaluated both recent and usual intake (Table 2). The two variables were highly correlated and gave similar results. Risk of breast cancer was increased approximately 70–80% among the most frequent consumers of alcohol (≥14 drinks per week), with no evidence of a dose-response gradient. The smoothed dose-response curve generated from the spline analysis (Figure 1) also indicated that the adverse effect of alcohol was restricted to the most frequent consumers.

Risk of breast cancer according to age when drinking was initiated, years since drinking began, and cumulative exposure are shown in Table 3. Women who started drinking in their teens had about the same risk of breast cancer as did women who started drinking later. Risk of

TABLE 1. Distribution of Potential Risk Factors and Associated Relative Risks (RRs) of Breast Cancer among Cases and Controls Younger than 45 Years of Age

Risk Factor	Cases (N)	Controls (N)	RR*	95% CI
Mother or sister with breast cancer				
No†	1,411	1,402	1.0	
Yes	233	95	2.42	1.9–3.1
Previous breast biopsy				
No†	1,484	1,404	1.0	
Yes	161	93	1.56	1.2–2.0
Menstrual status‡				
Premenopausal†	1,474	1,308	1.0	
Postmenopausal	171	187	0.73	0.6–0.9
Number of births				
≥4†	84	124	1.0	
3	221	240	1.38	1.0–1.9
2	597	503	1.80	1.3–2.4
1	336	297	1.74	1.3–2.4
0	407	333	2.03	1.5–2.8
Age (years) at first birth§				
<20†	220	255	1.0	
20–24	372	369	1.16	0.9–1.5
25–29	361	324	1.31	1.0–1.7
≥30	284	216	1.51	1.2–2.0
Age (years) at menarche				
≥14†	293	303	1.0	
13	442	444	1.03	0.8–1.3
12	512	402	1.31	1.1–1.6
≤12	396	346	1.18	0.9–1.5
Oral contraceptive use				
No†	388	430	1.0	
Yes (≥6 months)	1,257	1,067	1.31	1.1–1.5
Height (cm)‖				
<159†	333	350	1.0	
159–163	434	364	1.28	1.0–1.6
164–167	393	378	1.16	0.9–1.4
>167	454	380	1.39	1.1–1.7
Weight (kg)¶				
>77.6†	379	379	1.0	
66.1–77.6	408	373	1.13	0.9–1.4
58.4–66.0	419	377	1.17	1.0–1.4
<58.4	438	367	1.36	1.1–1.7
BMI (kg/m²)				
>29.9†	349	370	1.0	
24.7–29.9	399	365	1.19	1.0–1.5
21.9–24.6	381	370	1.12	0.9–1.4
<21.9	484	366	1.48	1.2–1.8

* Relative risks and 95% confidence intervals (95% CI) adjusted for age (continuous) and study site. For some variables, the number of observations does not equal 3,142 (1,645 cases and 1,497 controls) because of missing values.
† Referent category.
‡ Women who had not had a menstrual period during the 6 months before the interview were defined as postmenopausal; natural and surgical menopause were combined.
§ Restricted to parous women.
‖ Further adjusted for weight as a categorical variable.
¶ Further adjusted for height as a categorical variable.

the disease did not increase with increasing years since first use of alcohol. The total amount of alcohol consumed (that is, drink-years), however, was positively associated with risk (P for trend = 0.03). To determine whether the risk associated with cumulative intake was explained by its association with recent intake (Spearman $r = 0.65$), we examined the independent effect of each variable. Among drinkers, risk of breast cancer was 25% higher (95% CI = 0.9–1.2) among women in the highest category of cumulative intake (≥200 drink-years), compared with women in the lowest category (<50 drink-years). After controlling for recent intake, the effect estimate was reduced to 1.0 (95% CI = 0.6–1.6). Risk of the disease was 53% higher (95% CI = 1.0–2.3) among women who recently consumed ≥14 drinks per week compared with women who consumed <1 drink weekly. Controlling for cumulative intake did not materially alter the effect of recent consumption (RR = 1.5; 95% CI = 0.9–2.5). Hence, risk associated with cumulative intake was explained by recent consumption.

The effect of alcohol intake during different exposure periods is shown in Table 4. Few women regularly drank ≥14 drinks per week as teenagers; thus, ≥7 drinks per week was the highest category. Breast cancer risk was increased 34% (95% CI = 0.7–2.6) among women who consumed ≥7 drinks per week as teenagers. Risk was increased about 30% (95% CI = 0.9–2.0) among women who drank ≥14 drinks per week in their twenties and was increased 80% among women who consumed ≥14 drinks per week in their thirties (95% CI = 1.2–2.6).

Drinking in the thirties could not be disentangled from recent drinking because the two variables were so highly correlated (Spearman $r = 0.89$). Drinking in the twenties was less highly correlated with recent consumption (Spearman $r = 0.49$). The modest effect associated with drinking in the twenties was explained by contemporary intake. Among drinkers, risk of breast cancer was increased 19% (95% CI = 0.8–1.8) among women who consumed ≥14 drinks per week in their twenties compared with women who drank <1 drink weekly. After

TABLE 2. Relative Risks (RRs) of Breast Cancer According to Level of Alcohol Intake among Women Younger than 45 Years of Age

Alcohol Variable	Cases (N)	Controls (N)	RR*	95% CI
Recent intake (drinks/week)†				
Nondrinker‡	570	576	1.0	
<1	309	264	1.15	0.9–1.4
1–2.9	265	229	1.12	0.9–1.4
3–6.9	203	206	0.95	0.8–1.2
7–13.9	134	113	1.10	0.8–1.5
≥14	98	54	1.73	1.2–2.5
Drank before§	66	55	1.18	0.8–1.7
Usual intake (drinks/week)‖				
Nondrinker‡	570	576	1.0	
<1	203	150	1.35	1.1–1.7
1–2.9	344	327	1.01	0.8–1.2
3–6.9	300	277	1.03	0.8–1.3
7–13.9	140	119	1.10	0.8–1.5
≥14	88	48	1.79	1.2–2.6

* Adjusted for age, study site, race, parity, and oral contraceptive use.
† Five-year period up to the reference date.
‡ Referent category.
§ Drank only before recent interval (that is, before 5-year period before reference date).
‖ Average intake from start of drinking until reference date (includes any nondrinking years which occurred after drinking began).

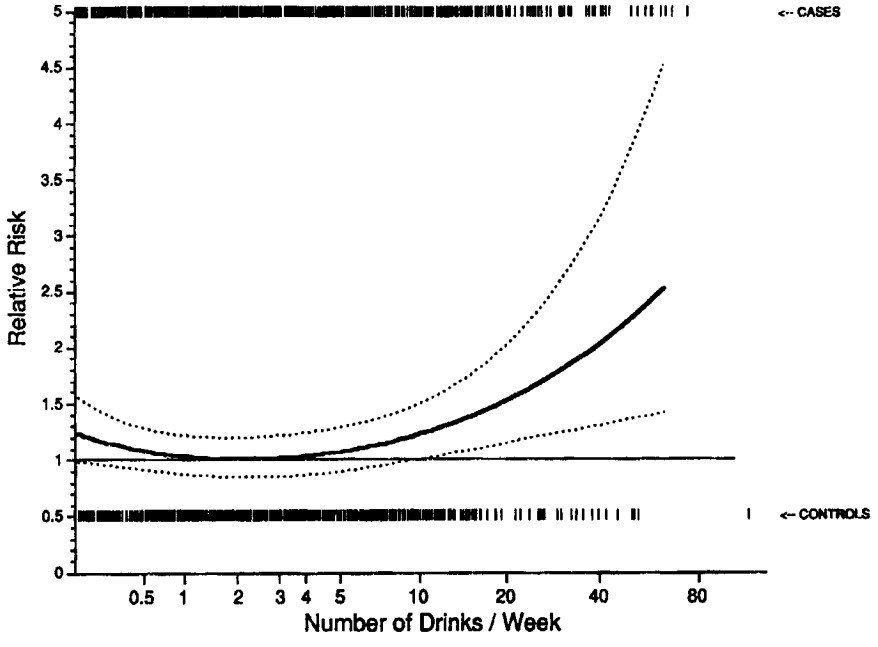

FIGURE 1. Fitted (2 degrees of freedom) natural cubic spline of breast cancer risk (*solid line*) and 95% CIs (*dashed lines*) according to recent alcohol consumption among women <45 years of age. Effect estimates are relative to nondrinkers. The *horizontal lines* at the top and bottom of the graph denote the distribution of cases and controls along the continuum of alcohol intake.

adjusting for recent intake, the corresponding RR was 0.92 (95% CI = 0.6–1.5). Controlling for intake in the twenties did not attenuate the risk associated with recent consumption of ≥14 drinks per week. The independent effects of teenage and recent alcohol consumption were difficult to evaluate because so few women were frequent consumers of alcohol during either period. Nevertheless, it appeared that the modest risk associated with teenage drinking was explained, in large part, by recent intake (Table 5). Within each category of teen drinking, breast cancer risk was highest among women in the top category of recent alcohol use.

TABLE 3. Relative Risks (RRs) of Breast Cancer According to Alcohol Usage Patterns and Index of Cumulative Exposure among Women Younger than 45 Years of Age

Alcohol Variable	Cases (N)	Controls (N)	RR*	95% CI
Age (years) started drinking				
Nondrinker†	570	576	1.0	
<17	88	114	0.81	0.6–1.1
17–79	412	337	1.19	1.0–1.4
≥20	575	470	1.15	1.0–1.4
Years since drinking began‡				
Nondrinker†	570	576	1.0	
<10	149	127	1.30	1.0–1.7
10–14	222	234	1.00	0.8–1.3
15–19	381	331	1.09	0.9–1.3
20+	323	229	1.20	1.0–1.5
Drink-years§				
Nondrinker†	570	576	1.0	
<50	554	512	1.08	0.9–1.3
50–99	238	210	1.07	0.8–1.3
100–149	108	76	1.31	0.9–1.8
150–199	57	42	1.25	0.8–1.9
≥200	118	81	1.35	1.0–1.8

* Adjusted for age, study site, race, parity, and oral contraceptive use.
† Referent category.
‡ Reference date minus age drinking began.
§ Average number of drinks per week (usual intake) multiplied by years since drinking began.

We examined the separate effects of beer, wine, and liquor (Table 6). Lifetime nondrinkers comprised the common referent group in these analyses. The two upper categories of recent alcohol consumption were collapsed because of small numbers. In multivariate analyses, the intake of alcohol from a specific type of beverage was adjusted for use of the other two types of beverages. The adverse effect of drinking was most pronounced for beer. After adjusting for other types of alcohol consumed, breast cancer risk was increased 2.6-fold (95% CI = 1.4–4.8) among women who recently consumed ≥7 beers per week. The corresponding effect estimate for wine was 1.5 (95% CI = 0.9–2.4), and for liquor it was 1.4 (95% CI = 0.7–2.8). These analyses were repeated using conversion factors[15] to estimate the amount of ethanol from beer (13 gm per 12 ounces), wine (11 gm per 4 ounces), and liquor (15 gm per 1.5 ounces); the effect estimates were similar. For example, after adjusting for intake of ethanol from wine and liquor, breast cancer risk was increased 2.4-fold (95% CI = 1.3–4.5) among women in the highest category of ethanol consumption (≥90 gm per week) from beer. The corresponding effect estimate for wine was 1.6 (95% CI = 0.9–3.1), and for liquor it was 1.6 (95% CI = 0.8–3.0).

To examine the possibility that the relation of breast cancer risk and alcohol intake was dependent on body size, we performed stratum-specific analyses. The effect estimates for recent drinkers (≥14 drinks per week) *vs* nondrinkers were: 1.7 (95% CI = 0.9–3.2) for a BMI of <23 (low weight-for-height), 1.3 (95% CI = 0.7–2.6) for a BMI of 23–27, and 1.6 (95% CI = 0.8–3.0) for a BMI >27 (excess weight-for-height). The results were

TABLE 4. Relative Risks (RRs) of Breast Cancer According to Level of Alcohol Intake for Three Exposure Periods among Women Younger than 45 Years of Age

Exposure Period and Average Intake (Drinks/Week)	Cases (N)	Controls (N)	RR*	95% CI
Teens				
Nondrinker†	570	576	1.0	
<1	311	273	1.11	0.9–1.4
1–2.9	124	125	1.00	0.8–1.3
3–6.9	43	35	1.28	0.8–2.0
≥7	22	18	1.34	0.7–2.6
Other times‡	575	470	1.15	1.0–1.4
Twenties				
Nondrinker†	570	576	1.0	
<1	251	222	1.11	0.9–1.4
1–2.9	310	276	1.06	0.9–1.3
3–6.9	238	212	1.09	0.9–1.4
7–13.9	127	97	1.24	0.9–1.7
≥14	59	46	1.29	0.9–2.0
Other times‡	90	68	1.28	0.9–1.8
Thirties§				
Nondrinker†	523	524	1.0	
<1	279	244	1.14	0.9–1.4
1–2.9	259	203	1.21	1.0–1.5
3–6.9	201	184	1.02	0.8–1.3
7–13.9	115	103	1.01	0.7–1.4
≥14	90	48	1.80	1.2–2.6
Other times‡	60	38	1.63	1.1–2.5

* Adjusted for age, study site, race, parity, and oral contraceptive use.
† Referent category.
‡ Nondrinker during specified exposure period but drank during other intervals.
§ Excludes women less than age 31 years at diagnosis (N = 271), since alcohol intake was truncated to reference date (that is, diagnosis age minus 2 years).

not materially altered when alcohol intake was expressed as number of drinks (or gm of ethanol) per kg of body weight (data not shown).

We also examined the effect of recent alcohol use according to disease stage (Table 7). The effect of alcohol was largely restricted to women with invasive disease (that is, local and regional/distant) and was most pronounced among women with the most advanced disease. Compared with nondrinkers, the risk estimates associated with recent intake of ≥14 drinks per week increased from 1.2 for *in situ* disease to 1.5 for local disease to 2.4 for regional/distant disease.

Because of concerns that excess risk associated with alcohol consumption might be related to more intensive screening, we examined the effect of common surveillance methods used at least 1 year before diagnosis or interview. Women who reported performing breast self-examinations were at somewhat reduced risk of breast cancer, whereas those who had a mammogram were at somewhat elevated risk. Among controls, alcohol use was more common among women who reported breast self-examinations than among women who did not examine themselves (62.0% *vs* 59.9%) and also was more common among controls who had mammograms than among those who had not been tested (65.8% *vs* 57.6%). The effect estimates associated with recent alcohol consumption were not materially altered after controlling for screening practices or when the analyses were restricted to women without screening (data not shown).

We assessed the possibility that the adverse effect of alcohol consumption might be related to detection bias. Methods by which cancers were first discovered included breast self-examination (34.2%), accidental self-discovery by either the patient or her partner (32.8%), routine mammography (19.3%), routine physical examination (8.2%), and other methods (5.5%). Tumors were more often detected by medical methods among drinkers compared with nondrinkers. For routine mammography, percentages in drinkers and nondrinkers were 20.2% *vs* 17.8%. For routine physical examinations, the percentages were 8.4% for drinkers and 7.6% for nondrinkers. Detection bias, however, is an unlikely explanation for the alcohol findings. For example, when we excluded from the analysis women whose tumors had been detected by mammography, recent consumption of ≥14 drinks per week continued to be associated with an increased risk (RR = 1.8; 95% CI = 1.2–2.7). Furthermore, the effect of recent alcohol intake was primarily restricted to women with invasive disease and was most pronounced among women with regional/distant disease. Very few women (7.6%) with advanced disease had their tumors detected by mammography.

TABLE 5. Relative Risks (RRs) of Breast Cancer According to Level of Recent Alcohol Intake within Strata of Alcohol Use during Teenage Years among Women Younger than 45 Years of Age

Exposure Period					
Teenage Years	Recent* Intake	Cases (N)	Controls (N)	RR†	95% CI
Lifetime nondrinker‡		570	576	1.0	
Drinker (drinks/week)					
<1	<3	182	155	1.13	0.9–1.4
	3–13.9	93	91	0.93	0.7–1.3
	≥14	19	12	1.32	0.6–2.8
1–2.9	<3	55	52	1.05	0.7–1.6
	3–13.9	43	58	0.73	0.5–1.1
	≥14	19	11	1.62	0.8–3.5
≥3	<3	16	16	1.01	0.5–2.1
	3–13.9	24	19	1.33	0.7–2.5
	≥14	15	11	1.52	0.7–3.4

* Five-year period before reference date.
† Adjusted for age, study site, race, parity, and oral contraceptive use.
‡ Referent category.

Discussion

In the present study, alcohol consumption was directly related to risk of breast cancer, but increased risk was concentrated among women who consumed ≥14 drinks per week. Contemporary drinking was more important than alcohol consumption in the past, indicating that alcohol may act at a relatively late stage. This finding was further supported by the observation that the association was largely restricted to women with invasive disease and was most pronounced among those with the most advanced disease.

TABLE 6. Relative Risks (RRs) of Breast Cancer According to Type of Alcohol-Containing Beverage Consumed Recently, with Intake of Each Beverage Type Adjusted for the Other Two in Multivariate Analyses among Women Younger than 45 Years of Age

Beverage	Recent Alcohol Intake from Specific Beverages (Drinks/Week)						
	None*	<0.5	0.5–0.9	1.0–2.9	3.0–6.9	≥7	Other†
Beer							
Control	576	235	78	125	66	38	324
Case	570	311	66	111	58	79	384
RR‡	1.0	1.26	0.81	0.89	0.88	2.07	1.11
RR§	1.0	1.24	0.87	0.85	0.74	2.57	
Wine							
Control	576	288	117	199	90	52	120
Case	570	345	135	207	104	92	126
RR‡	1.0	1.19	1.10	0.99	1.07	1.63	1.03
RR§	1.0	1.11	1.23	1.19	1.05	1.46	
Liquor							
Control	576	373	89	114	64	26	200
Case	570	427	117	129	72	46	218
RR‡	1.0	1.11	1.27	1.09	1.07	1.67	1.05
RR§	1.0	1.11	1.30	0.92	0.90	1.41	

* Lifetime nondrinker (referent category).
† Women who consumed none of the specified beverage (eg, beer) but did report other alcoholic beverage use (eg, wine and/or liquor).
‡ Adjusted for age, study site, race, parity, and oral contraceptive use.
§ Further adjusted for the amount of other alcohol consumed; indicator variables for beer, wine, and liquor (<1, 1–6.9, and ≥7, drinks per week).

Although our data did not indicate a dose-response gradient, we cannot completely rule out the possibility, given the width of the confidence intervals associated with the effect estimates for low levels of intake. The same cautionary note applies to several other investigations in which risk of breast cancer was not strongly elevated until women consumed at least 2–3 drinks daily.[5,16–18] A clear dose-response relation was observed in a recent multicenter case-control study including over 6,000 case subjects.[9]

In our study, drinking in the teens or twenties was not associated with risk of breast cancer. Poor recall of past drinking could have resulted in greater misclassification and attenuated risk estimates. Several studies, however, report that women accurately report alcohol consumption[19–21] and can provide reliable accounts of drinking in the remote past.[22] In the meta-analysis of Longnecker,[2] cohort studies with the longest follow-up periods had the lowest risk estimates, providing additional evidence that distant exposure may be less relevant than contemporary intake.

Further support for the hypothesis that alcohol acts at a late stage is provided by examining the alcohol-breast cancer association by disease stage. If alcohol, in fact, has no effect among women with *in situ* tumors but increases risk among women with advanced disease, then alcohol may act primarily as a tumor promoter or growth enhancer.

Few studies have evaluated the effect of duration of alcohol use or incorporated dose to consider the effect of cumulative exposure. Two groups[7,8,23] assessed age at first exposure to alcohol and did not find an association between duration of alcohol consumption and risk. In the only study to assess cumulative intake,[5] the investigators concluded that frequency of intake in the recent past was a more important determinant of risk than duration of the habit. Our findings confirm these observations.

Although several studies indicate that risk varies according to beverage type, no single beverage has been implicated consistently.[1,2] In the present study, effect estimates were highest among beer drinkers. Although beer drinking has been associated with breast cancer risk in a number of studies,[5,6,24–28] we found it difficult to assess the independent contributions of each beverage type. Women who drank tended to drink all types of alcohol-containing beverages. As suggested by Freudenheim,[28] risk associated with alcohol intake may be highest for the beverage most commonly used by heavy drinkers. Among controls who consumed ≥14 drinks per week, the median intake (drinks per week) of each beverage was 9.2 for beer, 3.4 for wine, and 1.4 for liquor. Although beer drinking may produce an effect beyond that of ethanol alone, beer consumption may also be associated with sociobehavioral differences not shared with wine and liquor consumption.[29]

At least three investigations indicate that the effect of alcohol is modified by body size.[3,24,27] In these studies, the adverse effect of alcohol appears either to be restricted to or most pronounced among thin women. Although it seems reasonable that a small or thin woman may receive a greater effective dose than a heavier woman consuming the same amount of alcohol, we saw no evidence of such effect-measure modification. Other

TABLE 7. Relative Risks (RRs) of Breast Cancer According to Level of Recent Alcohol Consumption by Stage of Breast Cancer at Diagnosis among Women Younger than 45 Years of Age

Recent Intake (Drinks/Week)	Stage of Breast Cancer at Diagnosis								
	In situ			Local			Regional/Distant		
	Case	RR*	95% CI	Case	RR*	95% CI	Case	RR*	95% CI
Nondrinker†	78	1.0		275	1.0		204	1.0	
<1	47	1.17	0.8–1.8	145	1.09	0.8–1.4	115	1.24	0.9–1.6
1–2.9	30	0.89	0.6–1.4	138	1.18	0.9–1.5	94	1.17	0.9–1.6
3–6.9	37	1.17	0.8–1.8	94	0.89	0.7–1.2	67	0.95	0.7–1.3
7–13.9	17	0.96	0.5–1.7	58	0.96	0.7–1.4	53	1.32	0.9–1.9
≥14	11	1.17	0.4–2.1	43	1.53	1.0–2.4	44	2.42	1.6–3.8

* Adjusted for age, study site, race, parity, and oral contraceptive use.
† Referent category.

studies also reported little evidence of effect-measure modification of alcohol consumption by body mass.[5,7,17,30]

Collecting information about alcohol exposure from cases after diagnosis raises concerns about recall bias. Two validation studies,[20,31] however, provide evidence that breast cancer cases and controls recall alcohol intake with similar accuracy. At the conclusion of the interview, we asked women what they thought caused breast cancer. Only 3.4% of cases and 2.9% of controls listed alcohol.

A variety of pathophysiologic mechanisms have been proposed for breast and other cancers.[32,33] Endogenous hormones, particularly estrogens, are thought to play a central role in the etiology of breast cancer.[34] Alcohol influences endocrine function, but relatively little is known about the effect of moderate alcohol consumption on estrogen metabolism. In the only controlled diet study of premenopausal women, moderate intake of ethanol (30 gm per day) was associated with increased total estrogen and the amount of bioavailable estrogen.[35]

In summary, this study adds further support to the accumulating evidence that alcohol intake is associated with increased risk of breast cancer. Our findings indicate that alcohol acts at a late stage in breast carcinogenesis. Our data do not support a dose-response gradient, and a biological mechanism has not been established, so that a causal inference is not clear-cut. Our results may not apply to older women, who comprise the majority of breast cancer cases and whose drinking habits may differ considerably from those of younger women. Although additional epidemiologic studies may eventually demonstrate a causal role of alcohol in the etiology of breast cancer, it may prove more useful to elucidate the relation between alcohol consumption and endogenous hormones.

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